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TITLE: Treating Intractable Post-Amputation Phantom Limb Pain with Ambulatory Continuous Peripheral Nerve Blocks

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13. SUPPLEMENTARY NOTES

14. ABSTRACT (brief – 200 words appro•.) of most significant finding during the research period.

This is a randomized, double-masked, placebo-controlled clinical trial. The results will not be available until the completion of enrollment and unmasking of treatment groups. Therefore, there are no results/findings to report at this juncture as we are still completing enrollment.

The tasks of the no-cost e•tension Year 5 encompassed continued recruiting, enrollment and data collection:

- 131 subjects enrolled to date for all centers
- 60 subjects provided crossover treatment
- Amputee support group outreach, prosthetics groups outreach, and clinic outreach conducted
- Data collection ongoing for all enrolled subjects
- We have but 13 subjects left to enroll to complete the study, and we would have enrolled these final subjects by the end of the no-cost e•tension Year 5 e•cept the hurricane that hit Puerto Rico this last summer knocked out the factory that makes the local anesthetic used in this study—ropivacaine—and, so our enrollment was halted because ropivacaine cannot be purchased in the United States. It is unclear when the factory will begin producing ropivacaine again; but, if it is not available by April 2018, we will consult with the Scientific Officer regarding the possibility of switching to a different long-acting local anesthetic—bupivacaine—for the final 13 subjects.
- The Department of Defense has approved a second no-cost e•tension year through December 24, 2018

15. SUBJECT TERMS

None listed

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
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Introduction:

This project is a randomized, double-masked, placebo-controlled, simultaneous parallel and crossover, human-subjects clinical trial to determine if ambulatory continuous peripheral nerve block (CPNB) is an effective treatment for intractable phantom limb pain following a traumatic limb amputation. There is currently no reliable treatment for phantom limb pain, which resolves in only 16% of cases. This is a multicenter trial at five collaborating sites: Walter Reed National Military Medical Center, Naval Medical Center San Diego, Veterans Affairs Palo Alto, Cleveland Clinic, and the University of California, San Diego. Subjects will have an e•isting upper or lower amputation and e•perience phantom limb pain at least 3 times each week for the previous 8 weeks. They will be randomized to receive one of two study solutions in a double-masked manner: either a local anesthetic (ropivacaine 0.5%) or placebo (normal saline). Catheters will be removed after 6 days of at-home infusion. Although not required, each subject has the option to return for the alternative treatment 4-16 weeks later (crossover infusion). The primary endpoint will be the difference in average phantom pain intensity at baseline and 4 weeks following the initial infusion as measured with the Numeric Rating Scale between treatment groups for the initial infusion. Secondary endpoints will involve intra- and inter-subject comparisons of additional measures of pain and health-related quality-of-life. This trial has a strong potential to identify the first reliably effective treatment for intractable phantom limb pain following a traumatic limb amputation.

Body:

Revised SOW (accepted November 2017 with approval of 2nd no-cost e•tension year):

Funding Year:	**2013**			**2014**	**2015**	**2016-17**	**2018**
Months (Within Year):	**1-4**	**5-8**	**9-12**				
Register study on clinicaltrials.gov	•						
Progress to date: The study was registered on clinicaltrials.gov prior to the beginning of enrollment.							
Initiate DSMB meetings	•						
Progress to date: Completed during the first year of the funding period.							
DSMB meetings (every 6 months)		•	•	•	•	•	•
Progress to date: The DSMB has met (by phone and/or SKYPE as the three members live in separate States) a total of two times since the previous annual report.							
Report to medical monitor (every month)		•	•	•	•	•	•
Progress to date: The Principal Investigator has provided a written report to the medical monitor Beverly Morris, RN (who is also the DSMB Chair), at the conclusion of each month; and, the medical monitor has confirmed receipt and approved the report each month. Information provided to the monitor monthly includes: the status of the study (new events such as how many institutions received IRB approval to send letters, interim analysis, personnel changes, etc); an enrollment update (currently enrolled, scheduled subjects for the following month, number left until next interim analysis); adverse events; unexpected adverse events; and							

protocol deviations.							
Finalize protocol and study forms	•						
Progress to date: This was completed during the first year of the funding period.							
Hire/train research coordinators	•	•	•				
Progress to date: This was completed during the first year of the funding period.							
Site visits and training by UCSD coordinator	•						
Progress to date: This was completed during the first year of the funding period.							
Submit study to individual IRBs and USAMRMC	•	•					
Progress to date: This was completed during the first year of the funding period.							
Site visits and training by Principal Investigator		•					
Progress to date: This was completed during the first year of the funding period.							
Prepare data-entry platform at UCSD	•						
Progress to date: This was completed during the first year of the funding period.							
Send database letters (following IRB approval)		•	•	•	•	•	
Progress to date: This was completed during the last year and was very successful.							
Educate clinic contacts for referrals		•	•				
Progress to date: This was completed during the first year of the funding period.							
Order and prepare equipment	•	•					
Progress to date: This was completed during the first year of the funding period.							
Amputee support group outreach			•	•	•	•	
Progress to date: This is ongoing for both of the centers continuing to enroll subjects: UC San Diego and the Cleveland Clinic.							
Advertising study in publications/websites			•	•	•	•	•
Progress to date: Advertising continues in three publications with nation-wide dispersion: InMotion, The O&P Edge, and Amplitude. This is the most successful way to reach potential subjects.							
Patient enrollment (following IRB approval)			•	•	•	•	•
Progress to date: We have enrolled 131 subjects with only 13 left to complete the study. We would have completed the study if not for the hurricane that hit Puerto Rico this last summer: the local anesthetic that we use—ropivacaine—is manufactured in Puerto Rico and has not been available since October 2017. Therefore, our enrollment is on hold until ropivacaine 0.4% again becomes available. The wholesalers do not know when the factory will be producing this medication again, so we cannot provide an anticipated date for restarting enrollment.							
Quality assurance			•	•	•	•	•
Progress to date: The research coordinators at each enrolling site upload their CRFs to the RedCap database and fax these same forms to us at UC San Diego. There is an individual associated with the study (IRB approved) who then checks every value against what is in RedCap to catch any errors. To date, we have found not a single error, which is a testament to the enrolling center research coordinators.							
Interim analyses (at 25%, 50%, 75% enrollment)					•	•	
Progress to date: The third and final interim analysis was completed during this past year and the DSMB recommended continuing with enrollment.							
Data collection & entry (Day 1 to Month 12)			•	•	•	•	•
Progress to date: Continues.							

Data cleaning and final statistical analysis							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
Abstract preparation							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
Full-length manuscript preparation							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
IRB closures at all enrolling centers							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
Final report to USAMRMC							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
Uploading results to ClinicalTrials.gov							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							
Results sent to all enrolled subjects							•
Progress to date: When the data collection has been completed, the data will be cleaned and analyzed. This cannot occur until enrollment is complete.							

DSMB: Data Safety Monitoring Board

UCSD: University of California San Diego

IRB: Institutional Review Board

USAMRMC: United States Army Medical Research and Materiel Command

Key Research Accomplishments:

We have enrolled all but 13 subjects in this multicenter clinical trial; and, we would have completed enrollment by this time e•cept that ropivacaine has become unavailable due to hurricane damage to the production factory in Puerto Rico. There are no study results to report at this time since this is a randomized, double-masked, placebo-controlled clinical trial; and, treatment group assignment will not be unmasked until the completion of enrollment.

Reportable Outcomes:

There are no reportable outcomes available at this time since this is a randomized, double-masked, placebo-controlled clinical trial; and, treatment group assignment will not be unmasked until the completion of enrollment.

Conclusion:

This is a randomized, triple-masked, placebo-controlled clinical trial that will remain masked until enrollment is completed and the final value for the primary endpoint has been collected. We are continuing enrollment; and, therefore, no results are available at this time.

References:
Non-applicable

Appendices:
None